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SHORT COMMUNICATION

Associations between depressive symptoms and insulin resistance: The Hoorn Study

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Abstract
Aims/hypothesis The association between depression and insulin resistance has been investigated in only a few studies, with contradictory results reported. The aim of this study was to determine whether the association between symptoms of depression and insulin resistance varies across glucose tolerance status and between men and women.
Subjects and methods Cross-sectional data from a population-based cohort study in Hoorn, a medium-sized town in the Netherlands, were analysed. The study sample consisted of 541 men and women aged 55–75 years, of whom 260 had NGT, 164 had IGT and 117 had established type 2 diabetes mellitus. Main outcome measures were insulin resistance defined by the homeostasis model assessment for insulin resistance (HOMA-IR) and symptoms of depression using the Centre for Epidemiologic Studies Depression Scale (CES-D).
Results In the total sample, we found a weak positive correlation between the depressive symptoms CED-D scores and HOMA-IR scores (r_s=0.156, p<0.001). Even weaker associations were found in subjects with NGT (r_s=0.041, p=0.509), in subjects with IGT (r_s=0.112, p=0.160) and in subjects with type 2 diabetes (r_s=0.007, p=0.942). The association between depressive symptoms and insulin resistance was similar for men and women.
Conclusions/interpretation We found only weak associations between depressive symptoms and insulin resistance, which did not differ among different glucose metabolism subgroups or between men and women.

Keywords Depressive symptoms · Hoorn Study · Insulin resistance · Population-based cohort

Abbreviations

CES-D	Centre for Epidemiologic Studies Depression Scale
HOMA-IR	homeostasis model assessment for insulin resistance
QUICKI	quantitative insulin sensitivity check index

Introduction

A recent meta-analysis of nine prospective epidemiological studies showed that depression is associated with an increased risk of incident type 2 diabetes [1]. The relationship between depression and insulin resistance is, however, less clear. So far three studies have reported on the association between depression and insulin resistance. A cross-sectional study by Lawlor and colleagues reported that depression was inversely related to insulin resistance

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among 4,268 British woman aged 60–79 years [2]. In contrast, a study by Timonen et al. in 491 male and female elderly Finnish individuals aged 61–63 years showed that insulin resistance and severity of depressive symptoms were positively correlated, particularly in people with IGT [3]. However, in a prospective cohort study, Lawlor and her colleagues concluded that reduced depressive symptoms were not associated with insulin resistance among 2,512 Welsh men aged 45–59 years [4].

These apparently contradictory results may be due to differences in methodology (longitudinal vs cross-sectional) and patient samples (men vs women). Of particular interest is whether the association between symptoms of depression with insulin resistance is different between men and women and across glucose tolerance status [5]. Therefore, we asked the following research questions: (1) Is a higher level of depression symptoms associated with increased insulin resistance in the total sample; and (2) does this association differ across glucose tolerance status and between sexes? We tested these hypotheses using cross-sectional data of a population-based cohort from The Hoorn Study.

Subjects and methods

Subjects The Hoorn Study is a population-based cohort study of type 2 diabetes in the general Dutch population. Details of the study have been described before [6]. In summary, it consisted of 2,844 men and women aged 50–75 years at baseline, selected from the population register of the medium-sized Dutch town of Hoorn. In 2000–2001, a third examination was performed among surviving participants who gave their permission to be re-contacted. We invited all participants who had diabetes, as determined by a 75-g OGTT or by diabetes treatment (n=176) at the second examination of the entire cohort in 1996–1998 [7]. We also invited random samples of participants who had NGT (n=705) or IGT (n=193) in 1996–1998. Of 1,074 individuals invited, 648 (60.3%) participated. The main reasons for not participating in the 2000–2001 follow-up examination are described elsewhere [8]. We assessed the cross-sectional relationship between depressive symptoms and insulin resistance in a cohort of 541 men and woman aged 55–75 years, of whom 260 had NGT, 164 IGT and 117 established type 2 diabetes mellitus. All subjects gave written informed consent and the Ethical Review Committee of the VU University Medical Centre approved the Study.

Methods All subjects underwent a single 75-g OGTT. Fasting glucose and 2-h post-load glucose after OGTT were measured in plasma with the hexokinase method (Roche Diagnostics, Mannheim, Germany). Glucose tolerance status was defined according to WHO 1999. Subjects were classified as having NGT, IGT (i.e. impaired fasting glucose or IGT), or type 2 diabetes mellitus.

Insulin resistance was estimated by the homeostasis model assessment for insulin resistance (HOMA-IR), calculated as (fasting insulin [in μU/ml] × fasting glucose [in mmol/l])/22.5, in line with Lawlor et al. [2, 4]. We also used the quantitative insulin sensitivity check index (QUICKI=1/[log (fasting insulin)+log (fasting glucose)]).

Symptoms of depression during the previous week were measured using the validated Dutch version of the 20-item Centre for Epidemiologic Studies Depression Scale (CES-D), with higher scores indicating more severe symptomatology. The Dutch translation of this instrument has been shown to have good psychometric properties and satisfactory criterion validity [9]. The CES-D total score can range from 0 to 60.

Analysis Descriptive statistics (means and 95% CIs) and correlations of the primary outcome measures CES-D and HOMA-IR in different glucose tolerance categories are presented. One-way ANOVAs were used to test whether CES-D and HOMA-IR scores differed between the three glucose status groups. Because of the skewed distribution of HOMA-IR scores, we used the non-parametric Spearman's rho to assess the association between depressive symptoms and insulin resistance. All analyses were performed separately for men and women. For all statistical testing, we used two-sided hypothesis testing with an alpha level of 0.05. Statistical analyses were performed using the SPSS 11.5 software package for Windows.

Results

Mean CES-D (p=0.002) and HOMA-IR (p<0.001) scores were significantly different between the three glucose status groups (Table 1). In the total sample, we found a weak positive correlation between the depressive symptoms CES-D scores and insulin resistance HOMA-IR scores (r_s=0.156, p<0.001; data not shown). Even weaker associations were found in subjects with NGT (r_s=0.041, p=0.509), in subjects with IGT (r_s=0.112, p=0.160) and in subjects with type 2 diabetes (r_s=0.007, p=0.942). The association between depressive symptoms and insulin resistance was not different for men and women. Finally, to make the analysis more robust we conducted a two-way ANOVA with sex and glucose tolerance status as independent variables and depression as the dependent variable. We found no significant interaction effect of sex × glucose tolerance status on depression (F=0.99; p=0.371).

Table 1 Correlations and means (95% CIs) of symptoms of depression (CES-D total scores) and homeostasis model assessment (HOMA-IR) in different glucose tolerance categories checked by OGTT in elderly Dutch subjects

	NGT (n=260)[a]	IGT (n=164)[b]	Type 2 diabetes (n=117)[c]
Correlation between HOMA-IR and CES-D			
Men and women			
r_s	0.041	0.112	0.007
p value	0.509	0.160	0.942
Men[d]			
n	129	84	54
r_s	0.033	0.072	−0.019
p value	0.712	0.517	0.891
Women			
n	129	75	61
r_s	0.063	0.101	−0.016
p value	0.478	0.389	0.901
Mean CES-D total scores (95% CI)	7.2 (6.4–7.9)	8.1 (7.1–9.0)	9.7 (8.4–11.0)[e]
Mean HOMA-IR scores (95% CI)	2.1 (2.0–2.2)	3.3 (3.0–3.5)	6.4 (5.4–7.5)[f]

[a] Fasting glucose <6.1 mmol/l and 2-h blood glucose <7.8 mmol/l in OGTT
[b] Fasting glucose ≥6.1 mmol/l and <7.0 mmol/l or 2-h blood glucose ≥7.8 and <11.1 mmol/l in OGTT
[c] Fasting glucose ≥7.0 mmol/l or 2-h blood glucose ≥11.1 mmol/l in OGTT
[d] Numbers may not total exactly because of missing data
[e] p=0.002, using one-way ANOVA
[f] p<0.001, using one-way ANOVA

Discussion

In the total sample, symptoms of depression and insulin resistance appeared to be only weakly associated. In addition, we found no evidence that this association is different for men and women or for people with different stages of disturbed glucose metabolism. The strengths of our study are that we used data from a large population-based sample of male and female subjects with documented glucose intolerance. Timonen et al. [3] used QUICKI, instead of the HOMA-IR scores used by Lawlor et al. [2, 4] and by us. However, in our study QUICKI and HOMA-IR had a perfect non-parametric correlation (r_s=−1.00). Likewise the rho correlations between QUICKI and depressive symptoms varied from −0.101 to 0.019. Therefore, we believe it is unlikely that the use of different definitions of insulin sensitivity or insulin resistance has seriously biased the results in the studies that have been conducted so far.

This study also had some limitations. For example, we used a self-report measure (CES-D) to assess symptoms of depression during the previous week, while the psychiatric diagnostic interview is the gold standard. However, the sensitivity of the CES-D to detect major depressive disorder is high [9]. In addition, the majority of subjects in our study had few symptoms indicative of depression. In our sample, 9% (24 of 271) of the men and 15% (41 of 270) of the women had a CES-D score ≥16, which is a generally accepted threshold for increased depression. As a result we could not test whether chronic or more severe depression is causally associated with insulin resistance. One could also question the validity of the HOMA-IR regarding the exact assessment of insulin resistance. The gold standard for measuring insulin resistance is the hyperinsulinaemic–euglycaemic glucose clamp technique, but this is not easy to apply in epidemiological studies. Yet several studies report that HOMA-IR scores correlate well with estimates from the euglycaemic clamp. Discrepancies in previous studies [2–4] may be explained by confounding by glucose status, which had not been determined.

The role of depression in the aetiology of insulin resistance and type 2 diabetes is not well understood. Further well-designed research is needed to establish the magnitude and direction of the relationship, particularly with regard to chronic symptoms of depression and development of insulin resistance and subsequent type 2 diabetes mellitus. Ideally, future population-based cohort studies should have a prospective design and include psychiatric diagnostic interviews, validated self-report depression measures and accurate insulin resistance measures (euglycaemic clamp data).

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Duality of interest The authors declare that there is no duality of interest.

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